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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,678	09/20/2006	Zhibing Hu	UNTD-0002 (122302.00085)	6923
7590 T Ling Chwang Jackson Walker 901 Main Street Suite 6000 Dallas, TX 75202-3797			EXAMINER ARIANI, KADE	
			ART UNIT 1651	PAPER NUMBER
			MAIL DATE 07/30/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/581,678	Applicant(s) HU ET AL.	
	Examiner Kade Ariani	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-47 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-47 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Claims 1-47 are pending in this application and were examined on their merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 15, 29, and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "substantially free" in claims 1, 15, 29, and 41, is indefinite because it is unclear what percentage of the "shell and core configuration" must be absent for the polymer to be considered substantially free from a shell & core polymer configuration, and what percentage of "oxygen gas" must be removed from isolated IPN nanoparticles to be considered substantially free from dissolved oxygen gas.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102() that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Kubota et al. (Journal of Applied Polymer Science, 1998, Vol. 70, p.1027-1034).

Claims 1- 10 are drawn to an aqueous dispersion of hydrogel nanoparticles comprising, interpenetrating polymer network (IPN) nanoparticles, a first polymer, poly (-N-isopropylacrylamide), a second polymer, poly (acrylic acid), and an aqueous medium, a drug, transformation from a low-viscous fluid to a gel when heated at about 34°C.

Kubota et al. discloses an aqueous dispersion of hydrogel nanoparticles comprising, IPN nanoparticles, a first polymer, poly (-N-isopropylacrylamide), a second polymer, poly (acrylic acid), and an aqueous medium, a drug, transformation from a low-viscous fluid to a gel when heated at about 34°C (see abstract and p. 1028 column 1, p.1029 Figure 1., p. 1033 column 2).

Kubota et al. therefore clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1- 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kubota et al. (Journal of Applied Polymer Science, 1998, Vol. 70, p.1027-1034) further in view of Kubota et al. (Journal of Applied Polymer Science, 2001, Vol. 80, p.789-805) and further in view of Gan & Lyon (J. Am. Chem. Soc., 2001, Vol. 123, No. 31, p.7511-7517) and further in view of Plucktaveesak et L. (XIIIth International Congress on Rheology, Cambridge, UK, 2000, 3-307-309) and further in view of Hennink & Nostrum (Advanced Drug Delivery, 2002, Vol. 13, p.13-36).

Claims 1- 28 are drawn to an aqueous dispersion of hydrogel nanoparticles comprising, interpenetrating polymer network (IPN) nanoparticles and a method of preparing an interpenetrating polymer network (IPN) comprising, providing a first mono-dispersed polymer nanoparticles prepared by mixing poly (-N-isopropylacrylamide (1st monomer), SDS (surfactant), N, N'-methylenebisacrylamide (1st cross linking agent), and potassium persulfate (1st initiator) at 70°C (1st temperature), adding poly (acrylic acid) (2nd monomer), N, N'-methylenebisacrylamide (2nd cross-linking agent), ammonium persulfate (2nd initiator), and TEMED (activator), mixing for about 120 minutes at 21°C (2nd temperature), isolating the IPN, mixing the isolated IPN with a biologically active material at a third temperature (about 33°C), uniformed sized hydrodynamic radius in the range of 75nm –200 nm, weight ratio of about 1:1.88, total polymer concentration from about 1.25 wt% to about 5.25 wt% in distilled water.

Claims 29-47 are drawn to cross-linked IPN nanoparticles and a method of preparing cross-linked IPNs nanoparticles comprising, providing IPN nanoparticles of poly(-N-isopropylacrylamide (1st polymer) interpenetrating poly(acrylic acid) (2nd

polymer), adding EDAC (1st cross-linking agent) and adipic acid dihydrazide (2nd cross linking agent) to IPN nanoparticles, heating the solution to about 44°C for 25-45 min (33-37 min), mixing cross-linked IPNs with a biologically active material at about 33°C, and average hydrodynamic radius in the range of 180-1000 nm (155-250 nm).

As mentioned immediately above, Kubota et al. teaches the limitations of claims 1-10. Kubota et al. also teaches a method of preparing an interpenetrating polymer network (IPN) comprising, providing a first mono-dispersed polymer nanoparticles prepared by mixing poly (-N-isopropylacrylamide (1st monomer), N, N'-methylenebisacrylamide (1st cross linking agent), and potassium persulfate (1st initiator) at 70°C (1st temperature), adding poly (acrylic acid) (2nd monomer), N, N'-methylenebisacrylamide (2nd cross-linking agent), ammonium persulfate (2nd initiator), and TEMED (activator), mixing for about 120 minutes at 21°C (2nd temperature), heating the solution to about 44°C, isolating the IPN, mixing the isolated IPN with a biologically active material at a third temperature (about 33°C), distilled water.

Kubota et al. does not teach SDS, the claimed reaction time, cross linking agents EDAC and adipic acid dihydrazide, weight ratio, total polymer concentration. However, Gan & Lyon teaches "the size of the particles was controlled via varying concentration of SDS during polymerization", and further teaches "higher concentrations of SDS result in smaller particle sizes as predicted by homogenous nucleation theory" (p.7512, column 2). Also, at the time the invention made, EDAC (a very efficient reagent to crosslink water-soluble polymers with amide bonds) to and adipic acid dihydrazide (for aldehyde-mediated crosslinking of polymers), were both being used as crosslinking

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agents for hydrogel preparation (Hennink & Nostrum, p. 19 column 1& Fig 4., p.20, column 1).

Moreover, at the time the invention was made it was very well known in the art that, "poly(N-isopropylacrylamide) gel in water undergoes a volume phase transition in response to temperature changes. This transition is dependent on the specific hydrophilic/hydrophobic balance (HLB) effects is sensitive to co-monomers incorporated into the network" (Kubota et al. 2001) and also "gelation temperature can be increased or decreased depending on the HLB of the surfactant" (Plucktaveesak et al. 2002).

Moreover, routine experimentation is widely used by one of ordinary skill in the art to determine optimum or workable ranges of particular parameters such as duration of the reaction, weight ratio, and polymer concentration. "[W] here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP Chapter 2100 – p.141).

Therefore, in view of the above teachings, it would have been obvious to one of the ordinary skill in the art to modify the method of Kubota et al. by adding SDS, and different cross linking agents. One would have been motivated to modify the method of Kubota et al. by adding SDS to change the size of the particles and as well as to increase or decrease the transition temperature of the hydrogel, and to obtain a more versatile drug release rate. Also, one would have been motivated to modify the method by using EDAC or adipic acid dihydrazide as crosslinking agents, in order to crosslink appropriate functional groups.

Accordingly, the invention taken as whole is *prima facie* obvious in view of the patents, applications and prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on 9:00 am to 5:30 pm EST Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

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USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kade Ariani
Examiner
Art Unit 1651



Leon B. Lankford Jr.
Primary Examiner
Art Unit 1651